molecule conjugate[, either in vitro,] or by catherization to the endothelial cells[, or during a surgical procedure involving the endothelial cells to be contacted].

12. (amended) The method of claim 1 wherein the conjugate is administered directly to the cells of to an individual in need of treatment or diagnosis.

13. (amended) A conjugate of an agent binding selectively to endothelial protein C receptor (EPCR) selected from the group consisting of protein C, activated protein C, antibodies reactive with EPCR and fragments thereof binding to EPCR, and a molecule to be delivered to a large vessel endothelial cell, wherein the molecule is not a diagnostic label, wherein the conjugate is a chemical conjugate, fusion protein or conjugate formed by indirect binding by a positively charged polymer, chimeric antibody or streptavidin.

16. (four times amended) The conjugate of claim 13 wherein the molecule to be delivered is a nucleic acid molecule in combination with means for directly contacting the nucleic acid molecule conjugate directly with the endothelial cells of large vessels, wherein the means are for in vitro treatment of the cells[, for] or by catherization to the endothelial cells[, or for performing a surgical procedure involving the endothelial cells to be contacted].

Remarks

Rejections under 35 U.S.C. §112

Claims 5, 6, 12 and and 16-18 were rejected under 35 U.S.C. §112, as non-enabled by the specification for *in vivo* delivery of genes to cells. Claims 5, 7, 16 and 19 were rejected under 35 U.S.C. §112, second paragraph, as indefinite. These rejections are traversed if applied to the amended claims.

As previously noted, copies of abstracts of work done in the same time period as when this application was filed have been submitted to demonstrate that those skilled in the art of gene

delivery were able to transfer genes as claimed, although different delivery systems. No evidence has been provided which demonstrates that the claimed conjugates would not be equally effective. Indeed, since soluble EPCR (although not a conjugate) circulates in the body and binds to endothelial cells, there is even more evidence that in the case using an EPCR-binding conjugate one would expect success. The examiner has failed to provide anything other than assertions to support his position as to the unpredictability of the claimed method. With regard to the statement that references submitted were postdated, it is not legally correct that they can be considered. These references are submitted as evidence that those of skill in the art could make and use the claimed method as of the time of filing. The references report on work that was on-going well prior to the filing date of this application, even though published post-filing.

Solely to facilitate prosecution without limiting the scope of the claims from which they depend, claims 5, 6, 12, and 16-18 have been amended to delete the objected to terms and to refer to direct administration to cells rather than individuals.

With regard to the phrase "non-nucleic acid drugs", the examiner's attention is drawn to page 2, lines 10-13. The specification there states "Molecules to be delivered can be nucleic acid, such as DNA, proteins such as transcription factors, diagnostic agents or other types of drugs." This provides implicit support for "non-nucleic acid" drugs, although should the examiner prefer, the language could be amended to recite "drugs other than nucleic acids and proteins".

The objected to language of claims 5, 7, 16 and 19 has been deleted.

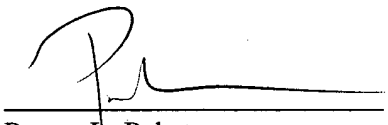
Rejections under 35 U.S.C. §102(b)

Claims 13, 15, 20 and 22 were rejected under 35 U.S.C. §102(e) as disclosed by U.S. patent No. 5,847,085 to Esmon. This rejection is respectfully traversed.

The claims have been amended to recite that the conjugate is a chemical conjugate, fusion protein or bound indirectly a positively charged polymer, chimeric antibody or streptavidin. Support is found at page 8, lines 9-17. Protein C and Protein S form a complex by ionic and hydrogen binding; not chemical conjugation.

Allowance of claims 1-25, as amended, is earnestly solicited. All claims as pending upon entry of this amendment are attached in an appendix to facilitate review by the examiner.

Respectfully submitted,



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Certificate of Mailing under 37 C.F.R. § 1.8(a)

I hereby certify that this Amendment, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: July 16, 2001

Patrea L. Pabst